

## Prior Authorization DRUG Guidelines

### **Alkeran (Melphalan)**

Effective Date: 10/22/13

Date Developed: 9/3/13 by Albert Reeves MD

Last Approval Date: 1/26/16, 1/24/17, 1/23/18, 1/22/19, 2/18/20,  
8/3/21, 2/1/22, 1/31/23, 2/13/24, 2/18/25

Melphalan is an antineoplastic/alkylating agent which chemically alters the [DNA](#) nucleotide [guanine](#) through [alkylation](#), and causes linkages between strands of DNA. This chemical alteration inhibits [DNA synthesis](#) and [RNA synthesis](#).

**Authorization Criteria:** Palliative treatment of multiple myeloma and non-resectable epithelial ovarian carcinoma; uveal melanoma (as a liver-directed therapy) in adults with unresectable hepatic metastases affecting <50% of the liver and no extrahepatic disease or extrahepatic disease limited to the bone, lymph nodes, SUBQ tissues, or lung that is amenable to resection or radiation.

**Off Label Use:** Amyloidosis, light chain; Hematopoietic cell transplant (allogeneic), reduced intensity conditioning regimen (hematologic malignancies); Hematopoietic cell transplant (autologous), conditioning regimen (lymphomas); Hodgkin lymphoma (relapsed or refractory); Regional perfusion in solid tumors (melanoma and soft tissue sarcoma)

**Dosing:** Multiple myeloma (palliative treatment):

**Note:** Response is gradual; may require repeated courses to realize benefit:

**Oral:** Usual dose (as described in the manufacturer's labeling):

6 mg once daily for 2-3 weeks initially, followed by up to 4 weeks rest, then a maintenance dose of 2 mg daily as hematologic recovery begins **or**

10 mg daily for 7-10 days; institute 2 mg daily maintenance dose after WBC

>4000 cells/mm<sup>3</sup> and platelets >100,000 cells/mm<sup>3</sup> (~4-8 weeks) titrate maintenance dose to hematologic response **or**

0.15 mg/kg/day for 7 days, with a 2–6-week rest, followed by a maintenance dose of ≤0.05 mg/kg/day as hematologic recovery begins **or**

0.25 mg/kg/day for 4 days (or 0.2 mg/kg/day for 5 days); repeat at 4- to 6-week intervals as ANC and platelet counts return to normal

**IV:** 16 mg/m<sup>2</sup> administered at 2-week intervals for 4 doses, then administer at 4-week intervals after adequate hematologic recovery.

**Note:** Intravenous melphalan is available in different formulations. Indications for use, product preparation, storage, and dosing differ between formulations. Use caution when selecting melphalan formulations for preparation and administration. Do not mix or combine the formulations. Antiemetics may be recommended to prevent nausea and vomiting; IV melphalan is associated with a moderate emetic potential. Adjust dose based on patient response and weekly blood counts.

**Ovarian carcinoma:** Oral: 0.2 mg/kg/day for 5 days, repeat every 4-5 weeks **or**

#### **Dosing: Adjustment for Possible Toxicity**

##### **Oral:**

WBC <3000/mm<sup>3</sup>: Withhold treatment until recovery

Platelets <100,000/mm<sup>3</sup>: Withhold treatment until recovery

**I.V.:** Adjust dose based on nadir blood cell counts

**Note:** Intravenous melphalan is available in different formulations. Indications for use, product preparation, storage, and dosing differ between formulations. Use caution when selecting melphalan formulations for preparation and administration. Do not mix or combine the formulations. Antiemetics may be recommended to prevent nausea and vomiting; IV melphalan is associated with a moderate emetic potential. Adjust dose based on patient response and weekly blood counts.

**How Supplied:** 2mg tablets

**Precautions:** nausea, vomiting, diarrhea; myelosuppression; hypersensitivity; renal toxicity; cardiotoxicity

**Note Boxed Warnings:** bone marrow suppression, hypersensitivity, leukemogenic

**Drug Interactions:** numerous, see product literature

hypertension, MI; with high-dose therapy), encephalopathy, hemolytic anemia, hemorrhagic cystitis, hepatic sinusoidal obstruction syndrome (SOS; veno-occlusive disease; high-dose I.V. melphalan), hepatitis, infection, injection site reactions (ulceration, necrosis), interstitial pneumonitis, jaundice, mucositis (with high-dose therapy), ovarian suppression, paralytic ileus (with high-dose therapy), pruritus, pulmonary fibrosis, radiation myelopathy, rash (maculopapular), renal toxicity (with high-dose therapy), seizure (with high-dose therapy), sepsis, SIADH, skin hypersensitivity, sterility, stomatitis, testicular suppression, tingling sensation, transaminases increased, vasculitis, warmth sensation

### **Contraindications**

Hypersensitivity to melphalan or any component of the formulation; patients whose disease was resistant to prior melphalan therapy

Bone marrow suppression: **[U.S. Boxed Warning]: Bone marrow suppression is common; may be severe and result in infection or bleeding; has been demonstrated more with the I.V. formulation (compared to oral).** Myelosuppression is dose related. Monitor blood counts; may require treatment delay or dose modification for thrombocytopenia or neutropenia. Use with caution in patients with prior bone marrow suppression, impaired renal function (consider dose reduction), or who have received prior (or concurrent) chemotherapy or irradiation. Myelotoxicity is generally reversible, although irreversible bone marrow failure has been reported. In patients who are candidates for autologous transplantation, avoid melphalan-containing regimens prior to transplant (due to the effects on stem cell reserve).

Hypersensitivity reactions: **[U.S. Boxed Warning]: Hypersensitivity reactions (including anaphylaxis) have occurred in ~2% of patients receiving I.V. melphalan,** usually after multiple treatment cycles. Discontinue infusion and treat symptomatically. Hypersensitivity may also occur (rarely) with oral melphalan. Do not readminister (oral or I.V.) in patients who experience hypersensitivity to melphalan.

Secondary malignancy: **[U.S. Boxed Warning]: Produces chromosomal abnormalities and is leukemogenic and potentially mutagenic.** Secondary malignancies (including acute myeloid leukemia, myeloproliferative disease, and carcinoma) have been reported (some patients were receiving combination chemotherapy or radiation therapy); the risk is increased with increased treatment duration and cumulative doses.

Experienced physician: **[U.S. Boxed Warning]: Should be administered under the supervision of an experienced cancer chemotherapy physician**

Severe hypersensitivity to pemetrexed or any component of the formulation

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Revision Date	Content Revised (Yes/No)	Contributors	Review/Revision Notes
1/24/17	No	Catherine Sanders, MD; Robert Sterling, MD	Annual review
1/23/18	No	Catherine Sanders, MD; Robert Sterling, MD	Annual review
1/22/19	No	Catherine Sanders, MD; Robert Sterling, MD	Annual review
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8/3/21	Yes	Howard Taekman, MD; Robert Sterling, MD	Added note under IV administration: Note: Intravenous melphalan is available in different formulations. Indications for use, product preparation, storage, and dosing differ between formulations. Use caution when selecting melphalan formulations for preparation and administration. Do not mix or combine the formulations. Antiemetics may be recommended to prevent nausea and vomiting; IV melphalan is associated with a moderate emetic potential. Adjust dose based on patient response and weekly blood counts.
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2/18/25	Yes	Howard Taekman, MD; Robert Sterling, MD	Added definition of Alkeran, removed Pharmaceutical category. Updated Authorization criteria and added Off Label Use.
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